REMARKS

Claim 1 has been amended to describe the inventive subject matter more clearly. Upon entry of the above amendments, claims 1-4, 6, 8, 11, and 21-37 are pending in the application.

The amendments do not introduce new matter within the meaning of 35 U.S.C. §132. Basis for the claim amendments is found on page 34, line 1 to page 42, line 20; in claim 1 as originally filed; and elsewhere throughout the specification and claims. Accordingly, entry of the amendments is respectfully requested.

INTERVIEW SUMMARY

Applicants take this opportunity to thank Examiners Owens and Geist for their courtesy and time in conducting an interview with Applicants' counsel on August 3, 2001. While agreement was not reached during the interview, the opportunity to discuss the outstanding rejections and to narrow the issues for appeal was appreciated.

1. Rejection of Claims 1-4, 6, 8, 11, and 21-37 under Judicially Created Doctrine of Obviousness-type Double Patenting

The Office Action rejects claims 1-4, 6, 8, 11, and 21-37 as being unpatentable over claims 7-10, 18-21, and 28-31 of U.S. Patent No. 5,786,378 (the '378 patent), under the judicially

created doctrine of obviousness-type double patenting. As the basis for this rejection, the Office Action states that although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to a method of effecting or treating neuronal activity in an animal with the same or analogous compounds. The Examiner concludes that the treatment of memory disorders and nerve-related vision disorders is thus *per se* obvious over the claims of the '378 patent.

Any obvious-type double patenting rejection should make clear: (A) the differences between the inventions defined by the conflicting claims, and (B) the reasons why a person of ordinary skill in the art would conclude that the claim in issue is an obvious variation of the claim in the patent or second application (MPEP §804, paragraph II.B.1). Further, the factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 U.S.P.Q. 459 (1966), for determining obviousness under 35 U.S.C. §103 should be employed when making an obviousness-type double patenting rejection (*In re Braat*, 937 F.2d 589, 19 U.S.P.Q.2d 1289, 1292 (Fed. Cir. 1991); MPEP § 804, paragraph II.B.1). The Office Action fails to discuss the differences between the purportedly conflicting claims and the *reasons* for concluding that the present claims are obvious variations of claims 19-33 of the '378 patent; the Examiner merely concludes, without stating any reasons, that methods for "treating

nerve-related vision disorders" and for "treating memory impairment" are methods for "effecting or treating neuronal activity."

Without waiving the aforementioned deficiencies, Applicants respectfully traverse the double patenting rejection on the ground that the instantly claimed invention is patentable over the invention claimed in the '378 patent.

A. Treating Vision Disorders Is Patentably Distinct from Effecting a Neuronal Activity

An obviousness-type double patenting rejection is improper where the application claims are patentably distinct from the prior patent claims. The '378 patent claims methods for "effecting a neuronal activity" (see claim 7). Contrary to the Office Action, the '378 patent does not claim methods for treating all "conditions which have a neurological basis".

Like *In re Kaplan*, 229 U.S.P.Q. 678 (Fed.Cir. 1986), the instant obviousness-type double patenting rejection involves earlier-filed, dominating claims ("effecting a neuronal activity" in the '378 patent) and later-filed improvement claims (the present claims to "treating a nerve-related vision disorder"). As Kaplan makes clear, *prima facie* evidence in support of an obviousness-type double patenting rejection must include "some clear evidence to establish why the variation would have been obvious which can properly qualify as 'prior art'," including prior art evidence of

the level of skill in the art if that is what the rejection is based upon (Id. at 683). However, the specification of the dominating patent **cannot** be used as prior art (Id. at 682, citing with approval *In re Vogel*, 164 U.S.P.Q. 619 (CCPA 1970).)

Like *In re Kaplan*, the only references cited in the Office Action to show that the presently claimed invention is an obvious variant of the '378 claimed invention are the '378 patent itself and the Applicants' specification. Lacking any other reference to support the rejection, it is clear that the Examiner has engaged in hindsight, using Applicants' specification to show obviousness. Thus, the Office Action fails to establish a *prima facie* case of obviousness-type double patenting in relation to vision disorders.

B. Treating Memory Disorders Is Patentably Distinct from Effecting a Neuronal Activity

The '378 patent claims methods for "effecting a neuronal activity" (see claim 7). Claim 8 of the '378 patent further specifies methods for "stimulation of damaged neurons, promotion of neuronal regeneration, prevention of neurodegeneration and treatment of neurological disorder." Claims 9 and 10 of the cited patent further claim treatment of the following specific neurological disorders: peripheral neuropathy caused by physical injury or disease state, physical damage to the brain, physical damage to the spinal cord, stroke associated with brain damage, and neurological disorders relating to neurodegeneration, specifically

Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis. Contrary to the Office Action, nowhere does the '378 patent claim a method for treating a memory disorder.

The present application claims methods of "treating memory impairment". Contrary to the Office Action, the present application does not claim "treating the neurological basis or etiology of ... memory impairment." While the Examiner contends that based on the '378 patent claims to "treating or effecting neuronal activity ... one of skill in the art would certainly have a reasonable expectation of success in the use of these compounds to treat conditions which have a neurological basis...", the Examiner does not provide the required factual or technical grounds establishing such relationship; the mere possibility or probability that a certain thing may result from a given set of circumstances is **not** sufficient. As discussed above, "some clear evidence to establish why the variation would have been obvious which can properly qualify as 'prior art'," must be shown; the Examiner's bare conclusion that there is a "reasonable expectation of success" is not a sufficient showing of prior art. Lacking any showing in the art of specific motivation to use the compounds claimed in the '378 patent in the methods of the present invention, the Office Action does not establish a *prima facie* case of obviousness.

Contrary to the Office Action, the art teaches that one cannot predict that compounds useful for treating diverse neurological conditions such as brain trauma, stroke, and the diseases of Alzheimer and Parkinson, would be effective for treating memory impairment. For example, the antidepressant Imipramine is useful in the treatment of Alzheimer's disease, but is not effective in treating the associated memory impairment. Teri et al., *J. Gerontol.*, 46 (1991) 372-377; copy enclosed. Similarly, Levodopa is useful in the treatment of Parkinson's disease, but does not affect the associated memory dysfunction. Owen et al., *Neuropsychologia*, 35 (1997) 519-532; copy enclosed.

At best, the '378 patent might make it obvious to try neurotrophic compounds for treating memory disorders. However, lacking any direction for selecting successful compounds or indication of critical parameters, this is insufficient to support a determination of obviousness. Thus, the Office Action fails to establish a *prima facie* case of obviousness-type double patenting in relation to memory disorders as well.

In the absence of any teaching or suggestion in the '378 patent that N-linked sulfonamides of heterocyclic thioester compounds used for treating neurological disorders would also be useful for treating nerve-related vision disorders or for treating memory impairment, the claims of the present application clearly are unobvious over the claims of the '378 patent.

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw this rejection.

2. Rejection of Claim 1 under 35 U.S.C. §112, first and second paragraphs

The Office Action rejects claim 1 under 35 U.S.C. §112, first and second paragraphs, because the rejected claim is vague and indefinite. The Examiner concludes that the language "heterocyclic ester" is overbroad.

Applicants first note that the Office Action inconsistently states that the rejection under 35 U.S.C. §112, first paragraph is withdrawn and maintained. As no basis for a rejection under this paragraph is stated, Applicants will rely on the statement in the Office Action that the rejection is withdrawn.

Applicants next note that the language "heterocyclic ester or amide" appeared in claim 1 as originally filed, but was replaced in the amendment dated November 16, 2000. Thus, this ground of rejection is moot.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

3. Rejection of Claims 1-4, 6, 8, 11, and 21-37 under 35 U.S.C. §103(a)

The Office Action rejects claims 1-4, 6, 8, 11, and 21-37 as being unpatentable over U.S. Patent Number 5,786,378 ("the '378 patent"). As the basis for this rejection, the Office Action states that the '378 patent teaches that the use of identical or analogous compounds "for the treatment of memory impairment." While admitting that the '378 patent does not teach treating vision disorders, the Examiner nevertheless argues that treating "neurological activity" in the '378 patent makes it *prima facie* obvious to treat nerve-related vision disorders.

Applicants respectfully traverse this rejection. The Examiner relies on his own generalizations to mischaracterize both the '378 patent and the present inventive subject matter. The '378 patent absolutely does **not** mention either memory impairment or vision disorders of any sort.

Applicants respectfully traverse the above rejection. The '378 patent does not teach or suggest Applicants' inventive subject matter as a whole, as recited in the amended claims. Further, the art teaches the ordinarily skilled artisan away from the subject matter as defined in the claims.

The U.S. Supreme Court in *Graham v. John Deere Co.*, 148 U.S.P.Q. 459 (1966) held that non-obviousness was determined under §103 by (1) determining the scope and content of the prior art; (2)

ascertaining the differences between the prior art and the claims at issue; (3) resolving the level of ordinary skill in the art; and, (4) inquiring as to any objective evidence of nonobviousness. In applying the *Graham* test, all of the facts must be considered; it is not acceptable within the framework of §103 to pick and chose from certain facts that support a position. Rather, all of the facts of the prior art and the instant invention must be taken into account.

A. The present inventive subject matter

Applicant's claims as presently amended are directed to a method for treating specified nerve-related vision disorders or treating memory impairment in an animal, which comprises administering to said animal an effective amount of a nitrogen-containing heterocyclic compound having two or more heteroatoms,

> wherein said compound has an N-linked substituent selected from the group consisting of -C(W)-C(Y)-
>
> > wherein W and Y are independently selected from the group consisting of O, S, CH_2, and H_2,
>
> wherein said compound is additionally substituted with a ester or amide substituent attached to the heterocyclic ring.

B. The prior art

As discussed above regarding the rejection under the

judicially created doctrine of obviousness-type double patenting, the '378 patent discloses a method for "effecting a neuronal activity" wherein the neuronal activity is selected from the group consisting of "stimulation of damaged neurons, promotion of neuronal regeneration, and treatment of neurological disorder". The '378 patent recites conditions such as peripheral neuropathy, physical damage to the brain, physical damage to the spinal cord, stroke associated with brain damage, Alzheimer's Disease, Parkinson's Disease, and amyotrophic lateral sclerosis as examples of such neurological disorders.

C. The differences between the claimed subject matter and the prior art

To establish a *prima facie* case, the PTO must satisfy three requirements. First, the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, must contain some suggestion or incentive that would have motivated the skilled artisan to modify a reference. *In re Fine*, 837 F.2d 1071, 1074, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988). Second the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1209, 18 U.S.P.Q.2d 1016, 1023 (Fed. Cir. 1991). Third, the prior art reference must teach or suggest all the limitations of the claims.

In re Wilson, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970).

In the present case, a legally sufficient *prima facie* case of obviousness must include a showing of the reasons why it would be obvious to use one or more reference compound(s) for the claimed utilities of the present invention. Here, the cited reference does not teach or suggest the use of any compound claimed in the present application for treating any form of memory impairment or for treating any type of vision disorders.

Treating Vision Disorders. For the reasons discussed above, whether denominated obviousness-type double patenting or obviousness under §103(a), improvement claims are not obvious over dominating patents. As *In re Kaplan* and *In re Fine* make clear, *prima facie* evidence in support of an obviousness-based rejection must include some clear prior art evidence to establish obviousness. Lacking any other cited reference(s), and in the absence of any teaching or suggestion in the '378 patent that the N-linked sulfonamides of heterocyclic thioester compounds used for treating neurological disorders would also be useful for treating vision disorders, the claims of the present application cannot be obvious over the '378 patent.

Treating Memory Disorders. While some of the conditions disclosed in the '378 patent may present with memory impairment as

one of their many symptoms, memory impairment can also occur in the absence of a disease or trauma, for example, as a consequence of age alone (see specification, pg. 21). Even where memory impairment manifests as a symptom of a neurological disorder, the etiology of the underlying disorder is often unknown. Without knowing how the claimed methods in either the '378 patent or the present application operate, or how the compounds used in the claimed methods elicit the desired effect, one cannot predict that compounds useful for treating a neurological disorder would be effective for treating memory impairment. For example, as discussed above, the antidepressant Imipramine is useful in the treatment of Alzheimer's disease, but is not effective in treating the associated memory impairment. Teri et al., *J. Gerontol.*, 46 (1991) 372-377; copy enclosed. Similarly, Levodopa is useful in the treatment of Parkinson's disease, but does not affect the associated memory dysfunction. Owen et al., *Neuropsychologia*, 35 (1997) 519-532; copy enclosed. Thus, in the absence of any teaching or suggestion in the '378 patent that the N-linked sulfonamides of heterocyclic thioester compounds used for treating neurological disorders would also be useful for treating memory impairment, the claims of the present application cannot be obvious over the '378 patent.

The discovery of a new use for an old compound based on unknown properties of the structure is patentable to the discoverer as a process of using. *In re Hack*, 245 F.2d 246, 248, 114 USPQ 161, 163 (CCPA 1957). In order to expedite prosecution and place the application in condition for allowance or appeal, Applicants have amended claim 1 to entirely exclude Alzheimer's disease and Parkinson's disease at this time (despite the fact that the art at the time the application was filed taught *only* that treating some non-memory aspects of multi-faceted diseases such as Alzheimer's and Parkinson's diseases does not treat associated memory impairment). These amendments are made without prejudice or disclaimer of any subject matter therein, and Applicants reserve the right to pursue any or all subject matter removed from this application in the restricted, canceled, or amended claims in a continuing application.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

CONCLUSION

Based upon the foregoing amendments and remarks, the presently claimed subject matter is definite, enabled, and patentably distinguishable over the art of record. The Examiner is therefore respectfully requested to reconsider and withdraw the rejections of

claims 1-4, 6, 8, 11, and 21-37 and allow pending claims 1-4, 6, 8, 11, and 21-37 presented herein for reconsideration. Favorable action with an early allowance of the pending claims is earnestly solicited.

The Examiner is invited to telephone the undersigned attorney if he has any questions or comments.

Respectfully submitted,

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